*Contains Nonbinding Recommendations*

**Draft Guidance on Amitriptyline Hydrochloride**



**Active ingredient:** Amitriptyline Hydrochloride

**Form/Route:** Tablet/Oral

**Recommended study:** 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 25 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments:

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 25 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments:

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**Analytes to measure (in appropriate biological fluid):** Amitriptyline, and its active metabolite, nortriptyline, in plasma

**Bioequivalence based on (90% CI):** Amitriptyline

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, please submit (i) individual and mean concentrations, (ii) individual and mean pharmacokinetic parameters, and (iii) geometric means and ratios of means for AUC and Cmax.

**Waiver request of in-vivo testing:** 10 mg, 50 mg, 75 mg, 100 mg, and 150 mg based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

**Dissolution test method and sampling times:**
**Please note that a Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.